Short report

The neurological complications of *Borrelia burgdorferi* in the New Forest area of Hampshire

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SUMMARY The neurological complications of *Borrelia burgdorferi* infection have only recently been recognised in the United Kingdom. Eight cases are reported which were all contracted in the New Forest area of Hampshire. The majority of patients had Bannwarth's syndrome though meningism and parenchymal lesions also occurred. All patients made a virtually complete neurological recovery in contrast to some patients with Lyme disease.

The neurological complications of *Borrelia burgdorferi* infection have only recently been recognised in the United Kingdom.¹ A similar neurological disorder, now also known to be often due to *B. burgdorferi* infection, has long been described in other parts of Europe (Bannwarth's syndrome)² and more recently in the United States (Lyme disease).³ Bannwarth described a group of patients with severe radicular pains, or lower motor neuron facial palsies, and a CSF lymphocytic pleocytosis which resolved spontaneously. The neurological manifestations of Lyme disease are similar though additional neurological abnormalities have been described.

The precise spectrum of the neurological complications of *B. burgdorferi* infection is unclear. Recent reports have suggested that acute transverse myelitis⁴ and chronic parenchymal neurological disease⁵ also occur. Differences in the neurological complications of *B. burgdorferi* infections may exist between Europe and the United States just as arthritis, another manifestation of *B. burgdorferi* infection, appears less common in Europe.⁶ Antigenic differences in the respective species of *B. burgdorferi* are known to exist and it has been suggested that they are responsible for these varied manifestations.⁷

Since we became aware of the neurological complications in the UK we have seen eight patients who contracted the disease in the New Forest area of Hampshire. We now report these cases to emphasise the occurrence of the disorder in this country and to draw attention to the type of neurological complications seen in the United Kingdom.

Clinical details of these eight patients are summarised in the table. The case histories of four patients are described in detail to illustrate the different types of neurological presentation.

Case reports

Patient 1 (Meningoencephalitis)⁸

Three weeks before his first admission this 9 year old boy was bitten on the back by a tick and within a few days developed an erythematous spreading skin eruption in the area of the tick bite. After 10 days the skin lesion subsided but this was accompanied by the onset of systemic symptoms. The child complained of malaise, generalised aches and pains, headache and abdominal pain. A few days before admission he developed dizziness, photophobia and vomiting. On admission he was unwell, but afebrile, with neck stiffness and a positive Kernig's sign. No rash was visible and there were no focal neurological signs. Routine haematological and biochemical investigations were negative. CSF examination showed turbid fluid with 1045 mononuclear cells/mm³ and a CSF glucose of 3.6 mmol/l. CSF culture for bacteria, fungi, and viruses was sterile and the CSF *treponeema pallidum* haemagglutination test was negative. Over the next 5 days the patient improved and was allowed home. However, he remained unwell with persistent malaise, head-

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Table Summary of the clinical features, outcome of treatment and serum *Borrelia burgdorferi* titres

Patient	Clinical Features	Tick bite	Erythema chronicum migrans	<i>B. burgdorferi</i> titre	Treatment and outcome
1	Chronic meningoencephalitis	+	+	1:1024	No treatment. Complete recovery No relapse
2	Bilateral facial palsy; dorsal and C8 radiculopathy; Chronic meningitis	—	—	1:1024	Oral penicillin. Complete recovery
3	Unilateral facial palsy; CSF not examined	+	—	≥ 1:256	Steroids and amoxycillin. Partial recovery
4	Unilateral facial palsy; radicular pains; CSF not examined	+	+	≥ 1:256	Steroids and oral tetracycline. Complete recovery
5	Unilateral facial palsy; radicular pains; dorsal numbness; CSF not examined	+	+	≥ 1:256	Oral tetracycline. Complete recovery
6	Bilateral facial palsy; chronic meningitis	—	+	≥ 1:256	Oral tetracycline and parenteral penicillin; complete recovery
7	Bilateral facial palsy; cerebellar syndrome; chronic meningitis	—	—	≥ 1:256	Steroids and parenteral penicillin. Persistent mild bilateral facial palsy, possible chronic neuropsychiatric syndrome
8	Lumbar radiculopathy; mild myelitis; chronic meningitis	—	—	≥ 1:256	Steroids and parenteral penicillin. Complete recovery

ache, dizziness and photophobia. On the morning of his second admission 2 weeks later, he was found confused in his bedroom with speech difficulty and right sided weakness. Examination showed an unwell boy who was afebrile but with marked neck stiffness. He had a nonfluent dysphasia with a mild right faciobrachial paresis. The fundi were normal. CT of the head showed no abnormality. The CSF contained 376 mononuclear cells/mm³, protein 2.1 g/l and glucose 2.8 mmol/l. CSF culture was again negative.

No treatment was given owing to doubts about the diagnosis. The dysphasia and right sided weakness resolved over the next 24 hours. Over the next 3 months the systemic symptoms and headaches gradually resolved without further neurological relapse. A diagnosis of *B. burgdorferi* infection was subsequently confirmed by a serum antibody titre of 1:1024.

Patient 2 (*Bannwarth's syndrome*)

This 59 year old woman discovered a tick on her lower abdomen when she got up one morning. She remained well for the next 5 weeks until she noticed a burning pain over her right eye and in her right arm. Two days later the right side of her face dropped and a few days later a rash appeared on her right upper thigh. Examination showed that she had a right lower motor neuron facial palsy and a rash compatible with erythema chronicum migrans. She was initially presumed to have a Bell's palsy and was treated with oral prednisolone (15 mg) daily, but when the rash appeared she received tetracycline. Whilst on treatment she continued to have burning pains in both arms, her chest and abdomen. Following treatment with tetracycline her rash faded almost immediately and her other symptoms resolved in a week. Her facial palsy did not begin to recover for another 2 weeks but then resolved within 1 week. She has remained well subsequently.

Patient 3 (*Bannwarth's syndrome; cerebellar syndrome*)

Three weeks before admission this 28 year old woman developed morning headache and vomiting which became gradually worse. After 10 days the headaches improved but she developed a left lower motor neuron facial palsy. Three days later she became sick and dizzy and developed a right lower

motor neuron facial palsy followed by some improvement in her systemic symptoms. There was no history of a tick bite or skin rash. Examination showed that she had bilateral lower motor neuron facial palsy and third degree rotatory nystagmus. She showed finger nose ataxia, incoordination of hand movements and a gait ataxia. Routine investigations were normal apart from an ESR of 26 mm/h. CT of the head and chest radiograph were normal. CSF contained 89 mononuclear cells/mm³ with an elevated protein of 1.4 g/l and no oligoclonal bands. She was treated with ACTH and the cerebellar syndrome improved within 24 hours. Despite subsequent improvement in the facial palsy she has permanent mild bilateral facial weakness. Since the original illness she has complained of persistent irritability, tension, depression, poor memory and concentration. Neuropsychological testing showed a pattern of cognitive deficit consistent with frontal and temporal lobe dysfunction rather than anxiety or depression. A 3 week course of intravenous penicillin and probenidol resulted in no improvement in these symptoms.

Patient 4 (*Bannwarth's syndrome, myelitis and possible peripheral nerve involvement*)

Three weeks before admission this 65 year old man developed pain in his right calf and numbness of the right foot. The intensity of the leg pain became gradually worse and he developed burning pain in the back of his thigh. The pain was especially severe at night. The right leg gradually became weaker over the next 2 weeks. There was no sphincter disturbance. There was no history of a tick bite or skin rash. Examination on admission showed that he had weakness of the right hip flexors and quadriceps with an absent right knee and ankle jerk and reduction of pin prick sensation in an S2 distribution on the right. The pain was very severe and required narcotic analgesics to control it. A myelogram showed no abnormality but CSF examination showed 288 mononuclear cells/mm³ with a protein of 1.5 g/l and a normal sugar. Two days later he deteriorated with weakness of dorsiflexion and inversion of the right foot and numbness of the left leg. Sensory examination now showed a sensory level to pin prick to T10 bilaterally. An EMG and nerve conduction study showed mild slowing of the distal

terminal motor velocities and an absent sural response but considerable prolongation of the F wave latencies. He was treated with a course of ACTH. The pain resolved in a few days and he made a gradual complete neurological recovery over the next 2 months. He did however develop new radicular symptoms during this period with band like pain around the upper chest and tingling along the ulnar borders of both forearms. Serum and CSF taken at the onset of his illness subsequently showed a serum titre for *B burgdorferi* of greater than 1:256 and a CSF titre of greater than 1:16.

Discussion

The commonest neurological presentation in this series of patients was a cranial neuropathy and/or painful radiculopathy (Bannwarth's syndrome). Facial palsy occurred in six patients and was bilateral in three. In one patient an apparent Bell's palsy was the only complication. No other cranial nerve palsies were seen. Four patients had radiculopathies, three of which were also associated with a facial palsy. They complained of severe pain and burning often in the chest or abdomen but also in the limbs. Motor weakness was a feature in only one of these patients.

Parenchymal involvement occurred in three patients. One child had a seizure, dysphasia and facio-brachial paresis which recovered in 24 hours. One patient suffered a cerebellar syndrome and another had a mild myelitis. Parenchymal involvement was generally mild and complete recovery always occurred. It never occurred alone; two cases were associated with Bannwarth's syndrome and the other had a chronic meningitis.

Three patients had meningeal symptoms or signs. All had a CSF pleocytosis but two other patients had a considerable CSF pleocytosis without meningeal symptoms. Generally the CSF showed a variable lymphocytosis (mean 353/mm³) with elevation of the protein (mean 2.1 g/l) and a normal glucose. The CSF IgG index was elevated and oligoclonal bands were detected in one patient but were absent in the only other patient whose CSF was sent for immunoelectrophoresis.

Although the major neurological complications of *B. burgdorferi* infection seen in the New Forest area of Hampshire are very similar to those described by Bannwarth (a cranial neuropathy or radiculopathy) important differences exist. Parenchymal involvement was a feature in three of our patients but did not occur in any of Bannwarth's patients. Meningeal symptoms and signs were prominent in almost half the present series whereas Bannwarth stressed their absence. In addition other European series of patients with Bannwarth's syndrome⁹ have had predominantly motor features in contrast to the sensory symptoms in ours.

Differences also exist from the neurological complications described in Lyme disease in which parenchy-

mal involvement has been reported to be a major feature, with a number of patients suffering irreversible neurological deficits¹⁰ whereas the patients in our series had only mild transient parenchymal involvement. In the USA myelitis is not described as a definite complication of Lyme disease.¹¹ However myelitis clearly does occur, since despite the much smaller experience of the disorder in Europe, one of our patients had cord involvement and a patient from Austria was recently described presenting with acute transverse myelitis.⁴ None of our patients developed new parenchymal lesions after their initial neurological illness which has been a feature of some American series.¹⁰

The prognosis is generally good. The majority of our patients made a complete recovery with or without treatment. Two patients have residual facial palsies, and one a possible neuropsychiatric syndrome. None of our patients has relapsed during the study (2 years).

The pathogenesis of the neurological complications is uncertain. It has been suggested that they are immunological¹² rather than due to the continued presence of the organism. However, the organism has been cultured from the CSF¹³ and there is good evidence that the meningeal features of the disease respond to parenteral penicillin.¹⁴ Also similar clinical features are seen in the course of other infections, for example tuberculous meningitis, which are known to be due to the presence of the organism. Although peripheral nerve involvement does occur in *B. burgdorferi* infection,¹⁵ this is generally mild in contrast to the severity of the radiculopathy. This is well illustrated by patient 4 whose nerve conduction studies showed mild distal slowing but considerable prolongation of the F wave latencies in keeping with the severe radiculopathy. These peripheral abnormalities may well be immunologically mediated but it seems likely that the common neurological manifestations of *B. burgdorferi* infection (Bannwarth's syndrome and a chronic meningitis) are due to the presence of the organism.

The best treatment of the neurological complications is uncertain. The disease is self limiting in some cases and one of our patients (No 1) who was severely affected made a complete recovery without treatment and has had no subsequent relapse. An American study¹⁴ suggested that the meningitic symptoms responded better to penicillin than steroids though some of the patients continued to have symptoms for a variable period after treatment and three of the penicillin group had been previously treated with steroids, making the study difficult to interpret. However, since the neurological complications are most likely to be due to the continued presence of the organism, we presently advise a 2 week course of intravenous penicillin 24 megaunits daily, together

with probenecid and measurement of the CSF penicillin levels to ensure that adequate levels are achieved. Culture of the organism in the UK and sensitivity testing should help guide antimicrobial therapy in the future.

Subsequent more chronic neurological complications of *B. burgdorferi* infection have recently been described. These have been called the tertiary stage of Lyme disease⁵: a chronic progressive encephalomyelitis has been reported in Europe¹⁶ and a multiple sclerosis like syndrome, psychiatric disease and severe chronic fatigue with subtle neurological signs in America.⁵ Optic neuritis¹⁷ and focal encephalitis¹⁸ have also been reported due to *B. burgdorferi*. No definite cases of chronic neurological *B. burgdorferi* infection have been seen in the New Forest area of Hampshire since we became aware of the possible diagnosis. The diagnosis of the chronic forms of neurological diseases due to borrelia infection rests on the finding of high antibody titres to *B. burgdorferi* and the exclusion of other neurological conditions. Coincidental borrelia infection may be commoner than is presently realised in endemic areas¹⁹ and serum antibody titres to *B. burgdorferi* may remain strongly positive for many years.¹⁰ Evidence of continuing active infection with a CSF pleocytosis and intrathecal synthesis of antibody to *B. burgdorferi* is required to be certain of the diagnosis in atypical cases. Future pathological verification would clearly help to establish that these more chronic forms of neurological disease are due to *B. burgdorferi* rather than other causes.

Erythema chronicum migrans and the neurological complications of *B. burgdorferi* infection occur in other parts of the British Isles.²⁰ The diagnosis should be considered in unexplained cranial polyneuropathy, painful radiculopathy and chronic lymphocytic meningitis. The absence of a history of a tick bite or skin rash does not exclude the diagnosis since only a proportion of patients report them. Examination of the CSF is helpful in the diagnosis since a lymphocytic pleocytosis is common if not invariable and the finding of oligoclonal bands and intrathecal antibodies to *B. burgdorferi* has been shown to be a feature of most cases in other studies.²¹ The sensitivity and specificity of present serological tests is uncertain and positive serum *B. burgdorferi* titres may occur in other spirochaetal infections, connective tissue disorders and possibly CNS lymphoma.²² Although our experience to date suggests that the incidence of positive antibody titres (> 1:256) to *B. burgdorferi* is negligible in the normal population, the finding of an elevated serum antibody titre to *B. burgdorferi* alone cannot, for the reasons given above, be regarded as sufficient proof that the neurological disorder is due to that organism.

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ADDENDUM

Since this paper was accepted for publication we have seen a further three patients with neurological complications due to *B. burgdorferi*. All three had Bannwarth's syndrome, that is a chronic lymphocytic meningitis with facial palsy and

severe radicular pain in the limbs; one patient also had a sixth nerve palsy. In two patients the *B. burgdorferi* titres were positive in the CSF but negative in the serum. Similar results have been described previously and emphasise the importance of estimation of CSF antibody titres in diagnosis. One patient who was allergic to penicillin was treated with oral tetracycline with an excellent clinical response. Concur-

rent CSF and serum IgG levels indicated breakdown of the blood brain barrier and although tetracycline does not penetrate well into the CSF, the rapid clinical recovery following the start of antibiotic treatment suggests that oral tetracycline may be an effective alternative to parenteral penicillin in the treatment of the neurological complications of *B. burgdorferi*.